Title

COMP-10. ANTI-CORRELATED TGFβ AND ALTERNATIVE END-JOINING DNA REPAIR SIGNATURES ASSOCIATE WITH OUTCOME IN PRIMARY GBM

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Presenter Application

Basic and Translational Brain Tumor Research Dinner Meeting
Wednesday, November 20, 2019
6:30–10:00pm, JW Marriott Hotel, Phoenix, Arizona

Yes, I would like to present at the EANO/SNO Basic and Translational Brain Tumor Research Dinner Meeting *(Submission deadline: Friday, May 20, 2019)*

Name: Mary Helen Barcellos-Hoff Degree(s) : Ph.D.

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Presentation Title: _____

I would like to present* in one the following areas:

- ○ Immunotherapy
- ○ Tumor Microenvironment, Angiogenesis and Epigenetics
- ○ Cell and Virus-based Therapies
- ○ Neuroimaging and Novel Technologies
- ○ CNS metastases
- ○ Cancer Stem Cells, Metabolism and Heterogeneity
- ○ Pediatric Tumors
- ◉ Novel Agents and Translational Approaches

○ Other category? _____

Enter your abstract here. Word limit 150 (no figures or tables please)

GBM generally exhibit high expression levels of transforming growth factor (TGFβ), its receptors and its target, tenascin. Cancer cells in which TGFβ signaling is compromised exhibit ineffective classical homologous combination and non-homologuos end-joining. As a consequence, DNA repair is primarily executed by an error-prone DNA repair pathway called alternative end-joining (altEJ), that is highly dependent on poly(ADP-ribose)polymerase (PARP). We determined that chronic TGFβ and altEJ transcriptional signatures are anti-corrleated (Pearson ' s correlation coefficient = -0.88, p<10-16) in GBM TCGA. Patients whose tumors exhibit the low TGFβ/high altEJ profile experience longer progression free survival (p<0.003) and overall survival (p<0.02) compared to those whose tumors have a high TGFβ/low altEJ profile. Preclinical data show that TGFβ inhibitor treatment of TGFβ competent GBM cell lines impairs classical DDR, thus forcing the cells to resort to altEJ and sensitizes to radiotherapy and PARP inhibition, providing strong rationale for translational studies.

SEND COMPLETED FORM TO LINDA GREER, linda@soc-neuro-onc.org or fax to 713-583-1345.

*Note: Submissions will be reviewed only for the purposes of presentation at the EANO/SNO Basic and Translational Brain Tumor Research Dinner, and will not be part of the main program for the SNO annual meeting nor published in the 2019 abstract supplement. *Oral Presentations are **5-minutes**, no more than 5 slides (without animation), PowerPoint file to be emailed to SNO by November 11, 2019*